

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: WALLACH, David
BIGDA, Jacek
BELETSKY, Igor
METT, Igor
ENGELMANN, Hartmut
- (ii) TITLE OF INVENTION: TNF INHIBITORS
- (iii) NUMBER OF SEQUENCES: 8
- (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: BROWDY AND NEIMARK
(B) STREET: 419 Seventh Street, N.W.
(C) CITY: Washington
(D) STATE: D.C.
(E) COUNTRY: USA
(F) ZIP: 20004
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: US 08/476,862
(B) FILING DATE: 07-JUN-1995
(C) CLASSIFICATION: 514
- (vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: IL 107267
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(A) APPLICATION NUMBER: IL 94039
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(A) APPLICATION NUMBER: IL 91229
(B) FILING DATE: 06-AUG-1989
- (vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: IL 90339
(B) FILING DATE: 18-MAY-1989
- (viii) ATTORNEY/AGENT INFORMATION:
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(B) REGISTRATION NUMBER: 25,618
(C) REFERENCE/DOCKET NUMBER: WALLACH=12A
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(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2224 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 90..1472

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GCGAGCGCAG CGGAGCCTGG AGAGAAGGCG CTGGGCTGCG AGGGCGCGAG GCGCGAGGGG	60
CAGGGGGCAA CCGGACCCCG CCCGCACCC ATG GCG CCC GTC GCC GTC TGG GCC	113
Met Ala Pro Val Ala Val Trp Ala	
1 5	
GCG CTG GCC GTC GGA CTG GAG CTC TGG GCT GCG GCG CAC GCC TTG CCC	161
Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro	
10 15 20	
GCC CAG GTG GCA TTT ACA CCC TAC GCC CCG GAG CCC GGG AGC ACA TGC	209
Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys	
25 30 35 40	
CGG CTC AGA GAA TAC TAT GAC CAG ACA GCT CAG ATG TGC TGC AGC AAA	257
Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys	
45 50 55	
TGC TCG CCG GGC CAA CAT GCA AAA GTC TTC TGT ACC AAG ACC TCG GAC	305
Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp	
60 65 70	
ACC GTG TGT GAC TCC TGT GAG GAC AGC ACA TAC ACC CAG CTC TGG AAC	353
Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn	
75 80 85	
TGG GTT CCC GAG TGC TTG AGC TGT GGC TCC CGC TGT AGC TCT GAC CAG	401
Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln	
90 95 100	
GTG GAA ACT CAA GCC TGC ACT CGG GAA CAG AAC CGC ATC TGC ACC TGC	449
Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys	
105 110 115 120	
AGG CCC GGC TGG TAC TGC GCG CTG AGC AAG CAG GAG GGG TGC CGG CTG	497
Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu	
125 130 135	
TGC GCG CCG CTG CGC AAG TGC CGC CCG GGC TTC GGC GTG GCC AGA CCA	545
Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro	
140 145 150	
GGA ACT GAA ACA TCA GAC GTG GTG TGC AAG CCC TGT GCC CCG GGG ACG	593
Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr	
155 160 165	
TTC TCC AAC ACG ACT TCA TCC ACG GAT ATT TGC AGG CCC CAC CAG ATC	641
Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile	
170 175 180	
TGT AAC GTG GTG GCC ATC CCT GGG AAT GCA AGC ATG GAT GCA GTC TGC	689
Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys	
185 190 195 200	
ACG TCC ACG TCC CCC ACC CGG AGT ATG GCC CCA GGG GCA GTA CAC TTA	737
Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu	
205 210 215	

[illegible]

CTGACCTGCA GGCCAAGAGC AGAGGCAGCG AGTTGGGGAA AGCCTCTGCT GCCATGGTGT 1692
 GTCCCTCTCG GAAGGCTGGC TGGGCATGGA CGTTCGGGGC ATGCTGGGGC AAGTCCCTGA 1752
 CTCTCTGTGA CCTGCCCCGC CCAGCTGCAC CTGCCAGCCT GGCTTCTGGA GCCCTTGGGT 1812
 TTTTGTGTTG TTTGTTTGTT TGTGTTGTTG TTTCTCCCCC TGGGCTCTGC CCAGCTCTGG 1872
 CTTCCAGAAA ACCCCAGCAT CCTTTTCTGC AGAGGGGCTT TCTGGAGAGG AGGGATGCTG 1932
 CCTGAGTCAC CCATGAAGAC AGGACAGTGC TTCAGCCTGA GGCTGAGACT GCGGGATGGT 1992
 CCTGGGGCTC TGTGTAGGGA GGAGGTGGCA GCCCTGTAGG GAACGGGGTC CTTCAAGTTA 2052
 GCTCAGGAGG CTTGGAAAGC ATCACCTCAG GCCAGGTGCA GTGGCTCACG CCTATGATCC 2112
 CAGCACTTTG GGAGGCTGAG GCGGGTGGAT CACCTGAGGT TAGGAGTTCG AGACCAGCCT 2172
 GGCCAACATG GTAAACCCC ATCTCTACTA AAAATACAGA AATTAGCCGG GC 2224

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 461 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
 1 5 10 15
 Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
 20 25 30
 Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
 35 40 45
 Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
 50 55 60
 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
 65 70 75 80
 Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
 85 90 95
 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
 100 105 110
 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
 115 120 125
 Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
 130 135 140
 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
 145 150 155 160
 Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
 165 170 175

Asp	Ile	Cys	Arg	Pro	His	Gln	Ile	Cys	Asn	Val	Val	Ala	Ile	Pro	Gly	180	185	190
Asn	Ala	Ser	Met	Asp	Ala	Val	Cys	Thr	Ser	Thr	Ser	Pro	Thr	Arg	Ser	195	200	205
Met	Ala	Pro	Gly	Ala	Val	His	Leu	Pro	Gln	Pro	Val	Ser	Thr	Arg	Ser	210	215	220
Gln	His	Thr	Gln	Pro	Thr	Pro	Glu	Pro	Ser	Thr	Ala	Pro	Ser	Thr	Ser	225	230	235
Phe	Leu	Leu	Pro	Met	Gly	Pro	Ser	Pro	Pro	Ala	Glu	Gly	Ser	Thr	Gly	245	250	255
Asp	Phe	Ala	Leu	Pro	Val	Gly	Leu	Ile	Val	Gly	Val	Thr	Ala	Leu	Gly	260	265	270
Leu	Leu	Ile	Ile	Gly	Val	Val	Asn	Cys	Val	Ile	Met	Thr	Gln	Val	Lys	275	280	285
Lys	Lys	Pro	Leu	Cys	Leu	Gln	Arg	Glu	Ala	Lys	Val	Pro	His	Leu	Pro	290	295	300
Ala	Asp	Lys	Ala	Arg	Gly	Thr	Gln	Gly	Pro	Glu	Gln	Gln	His	Leu	Leu	305	310	315
Ile	Thr	Ala	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Leu	Glu	Ser	Ser	Ala	Ser	325	330	335
Ala	Leu	Asp	Arg	Arg	Ala	Pro	Thr	Arg	Asn	Gln	Pro	Gln	Ala	Pro	Gly	340	345	350
Val	Glu	Ala	Ser	Gly	Ala	Gly	Glu	Ala	Arg	Ala	Ser	Thr	Gly	Ser	Ser	355	360	365
Asp	Ser	Ser	Pro	Gly	Gly	His	Gly	Thr	Gln	Val	Asn	Val	Thr	Cys	Ile	370	375	380
Val	Asn	Val	Cys	Ser	Ser	Ser	Asp	His	Ser	Ser	Gln	Cys	Ser	Ser	Gln	385	390	395
Ala	Ser	Ser	Thr	Met	Gly	Asp	Thr	Asp	Ser	Ser	Pro	Ser	Glu	Ser	Pro	405	410	415
Lys	Asp	Glu	Gln	Val	Pro	Phe	Ser	Lys	Glu	Glu	Cys	Ala	Phe	Arg	Ser	420	425	430
Gln	Leu	Glu	Thr	Pro	Glu	Thr	Leu	Leu	Gly	Ser	Thr	Glu	Glu	Lys	Pro	435	440	445
Leu	Pro	Leu	Gly	Val	Pro	Asp	Ala	Gly	Met	Lys	Pro	Ser				450	455	460

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 153 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys
1 5 10 15
Cys Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly
20 25 30
Pro Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr
35 40 45
Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser Lys Cys Arg
50 55 60
Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp Arg Asp
65 70 75 80
Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu
85 90 95
Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val
100 105 110
His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala
115 120 125
Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys
130 135 140
Lys Ser Leu Glu Cys Thr Lys Leu Cys
145 150

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 163 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys
1 5 10 15
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
20 25 30
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
35 40 45
Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Asp
50 55 60
Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
65 70 75 80
Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
85 90 95
Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
100 105 110
Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
115 120 125

Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
 130 135 140
 Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala
 145 150 155 160
 Val Cys Thr

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 119 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Gln Asn Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro
 1 5 10 15
 Cys Pro Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp
 20 25 30
 Glu Pro Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys
 35 40 45
 Ala His Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly
 50 55 60
 His Gly Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys
 65 70 75 80
 Cys Arg Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His
 85 90 95
 Cys Asp Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr
 100 105 110
 Leu Thr Ser Asn Thr Lys Cys
 115

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 159 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Ala Cys Pro Thr Gly Leu Tyr Thr His Ser Gly Glu Cys Cys Lys Ala
 1 5 10 15
 Cys Asn Leu Gly Glu Gly Val Ala Gln Pro Cys Gly Ala Asn Gln Thr
 20 25 30
 Val Cys Glu Pro Cys Leu Asp Ser Val Thr Ser Ser Asp Val Val Ser
 35 40 45

Ala Thr Glu Pro Cys Lys Pro Cys Thr Glu Cys Val Gly Leu Gln Ser
50 55 60

His Ser Ala Pro Cys Val Glu Ala Asp Asp Ala Val Cys Arg Cys Ala
65 70 75 80

Tyr Gly Tyr Tyr Gln Asp Glu Thr Thr Gly Arg Cys Glu Ala Cys Arg
85 90 95

Val Cys Glu Ala Gly Ser Gly Leu Val Phe Ser Cys Gln Asp Lys Gln
100 105 110

Asn Thr Val Cys Glu Glu Cys Pro Asp Gly Thr Tyr Ser Asp Glu Ala
115 120 125

Asn His Val Asp Pro Cys Leu Pro Cys Thr Val Cys Glu Asp Thr Glu
130 135 140

Arg Gln Leu Arg Glu Cys Thr Arg Trp Ala Asp Ala Glu Cys Glu
145 150 155

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 162 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Ala Cys Arg Glu Lys Gln Tyr Leu Ile Asn Ser Gln Cys Cys Ser Leu
1 5 10 15

Cys Gln Pro Gly Gln Lys Leu Val Ser Asp Cys Thr Glu Phe Thr Glu
20 25 30

Thr Glu Cys Leu Pro Cys Gly Glu Ser Glu Phe Leu Asp Thr Trp Asn
35 40 45

Arg Glu Thr His Cys His Gln His Lys Tyr Cys Asp Pro Asn Leu Gly
50 55 60

Leu Arg Val Gln Gln Lys Gly Thr Ser Glu Thr Asp Thr Ile Cys Thr
65 70 75 80

Cys Glu Glu Gly Trp His Cys Thr Ser Glu Ala Cys Glu Ser Cys Val
85 90 95

Leu His Arg Ser Cys Ser Pro Gly Phe Gly Val Lys Gln Ile Ala Thr
100 105 110

Gly Val Ser Asp Thr Ile Cys Glu Pro Cys Pro Val Gly Phe Phe Ser
115 120 125

Asn Val Ser Ser Ala Phe Glu Lys Cys His Pro Thr Ser Cys Glu Thr
130 135 140

Lys Asp Leu Val Val Gln Gln Ala Gly Thr Asn Lys Thr Asp Val Val
145 150 155 160

Cys Gly

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 140 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Asn	Cys	Val	Lys	Asp	Thr	Tyr	Pro	Ser	Gly	His	Lys	Cys	Cys	Arg	Glu	1	5	10	15
Cys	Gln	Pro	Gly	His	Gly	Met	Val	Ser	Arg	Cys	Asp	His	Thr	Arg	Asp	20	25	30	
Thr	Val	Cys	His	Pro	Cys	Glu	Pro	Gly	Phe	Tyr	Asn	Glu	Ala	Val	Asn	35	40	45	
Tyr	Asp	Thr	Cys	Lys	Gln	Cys	Thr	Gln	Cys	Asn	His	Arg	Ser	Gly	Ser	50	55	60	
Glu	Leu	Lys	Gln	Asn	Cys	Thr	Pro	Thr	Glu	Asp	Thr	Val	Cys	Gln	Cys	65	70	75	
Arg	Pro	Gly	Thr	Gln	Pro	Arg	Gln	Asp	Ser	Ser	His	Lys	Leu	Gly	Val	85	90	95	
Asp	Cys	Val	Pro	Cys	Pro	Pro	Gly	His	Phe	Ser	Pro	Gly	Ser	Asn	Gln	100	105	110	
Ala	Cys	Lys	Pro	Trp	Thr	Asn	Cys	Thr	Leu	Ser	Gly	Lys	Gln	Ile	Arg	115	120	125	
His	Pro	Ala	Ser	Asn	Ser	Leu	Asp	Thr	Val	Cys	Glu	130	135	140					